REMARKS

Claims 1-13 are pending in the application. The claims have not been amended by the present response.

It is applicants' understanding that the present Office Action is a non-final action. Both the Office Action Summary and public PAIR state that the action is non-final. However, paragraph 5 at page 4 of the Office Action states that the action is made final. It is applicants' understanding that the status as marked in the Office Action Summary and at public PAIR reflect the correct status of the Office Action.

Allowable Subject Matter

At page 4 of the Office Action, the Examiner stated that claims 3-5 and 11-13 are allowed. In view of the remarks presented herein, applicants respectfully submit that all of the pending claims are in condition for allowance.

35 U.S.C. §112, First Paragraph (Written Description)

At pages 2-4 of the Office Action, claims 1, 2, and 6-10 were rejected as containing subject matter that was not described in the specification in such a way that one skilled in the art can reasonably conclude that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully traverse the rejection in view of the following remarks.

As detailed in the response to the previous Office Action, the present application describes the identification and characterization of two species of RetL3 proteins: the human RetL3 protein (SEQ ID NO:21); and the mouse RetL3 protein (SEQ ID NO:17). These two species of RetL3 are 76.8% identical to each other. The alignment of the amino acid sequences of the two RetL3 proteins provided in the prior response identified both (i) those amino acid residues that are identical between the human and mouse wild-type RetL3 proteins, and (ii) those amino acid residues that differ between the two species. The skilled artisan would readily expect that, at a minimum, those particular amino acids that differ between the two wild-type RetL3

proteins (i.e., 23.2% of the amino acid positions) are likely to be amenable to change without eliminating biological activity. Similarly, those amino acids that do not differ between the two species are more likely to be associated with domains or motifs that are required for the maintenance of RetL3 function. It is the provision in the specification of the amino acid sequences of these two divergent species of wild-type RetL3 proteins that allows a person of ordinary skill in the art to readily identify specific amino acids that can likely be changed without destroying the ability of a variant RetL3 polypeptide to interact with the receptor tyrosine kinase Ret.

Independent claim 1 is directed to an isolated polypeptide that (i) comprises an amino acid sequence that is at least 80% identical to the sequence of SEQ ID NO:17 or SEQ ID NO:21, and (ii) interacts with and triggers dimerization or autophosphorylation of the receptor protein Ret. The genus of polypeptides encompassed by claim 1 does not have substantial variation, since all such polypeptides must have a specified activity and contain a sequence that is at least 80% identical to SEQ ID NO:17 or SEQ ID NO:21. As noted above, the human and mouse RetL3 proteins disclosed in the specification are representative of the claimed genus because: all polypeptides encompassed by the claimed genus are required to be even more closely related (i.e., at least 80%, 90%, or 95% identical) to SEQ ID NO:17 or SEQ ID NO:21 than the variation (76.8% identity) that exists between the two RetL3 species exemplified in the application; and routine assays are well known in the art for identifying variants having the functional activity specified by the claim. As compared to the specification's disclosure of two species of RetL3 proteins that are 76.8% identical to each other, pending claims 1, 2, and 6-10 encompass variation that is less than the variation existing between the two disclosed RetL3 proteins.

The present Office Action responds to applicants' sequence comparison remarks by stating that "the two species Applicants' point out, human RetL3 (SEQ ID NO: 21) and the murine RetL3 (SEQ ID NO: 17) only share 76.8% identity and do not share at least 80% identity as the claims read on so they are not reliable species to base arguments upon" (emphasis added). Applicants strongly contest the logic underlying the Office Action's argument reproduced above. Because the two disclosed species of RetL3 proteins differ at 23.2% of their amino acids, the

skilled artisan would immediately recognize 23.2% of the amino acid residues of either SEQ ID NO:21 or SEQ ID NO:17 that could likely be changed and result in a polypeptide that retains the ability to interact with and trigger dimerization or autophosphorylation of Ret. The disclosure of two RetL3 species that are 76.8% identical means that there is sufficient description of polypeptides that exhibit a percent identity of 76.8% or higher with respect to the sequence of SEQ ID NO:21 or SEQ ID NO:17. In contrast, the Examiner appears to regard the 76.8% identity as being too low to support the written description of claims that recite 80% (or 90% or 95%) identity. Applicants respectfully request reconsideration of that position. Following the standard applied by the Examiner, it is unclear what species relatedness would satisfy the Examiner that the claimed subject matter is adequately described. Surely the provision of two functional RetL3 species that are 76.8% identical is more relevant to the written description of the claims than two hypothetical species that are, say, 98% identical. Is it the Examiner's position that two RetL3 species that are 98% identical would somehow be "reliable species to base arguments upon" and that the disclosed RetL3 species would not? Clearly, such a hypothetical disclosure would be significantly less useful than that of the present application at identifying 20% of the amino acid residues (i.e., for those claims that recite 80% identity) of SEQ ID NO:21 or SEQ ID NO:17 that are likely to be amenable to change without eliminating RetL3 biological activity. If the Examiner intends to maintain the present rejection, applicants respectfully request clarification as to how the 76.8% identity between the two disclosed RetL3 species renders them "unreliable" to base written description arguments upon.

In view of the foregoing remarks, applicants respectfully submit that the skilled artisan would have concluded that the inventors were in possession (at the time of filing of the present application) of the necessary common attributes possessed by the members of the claimed genus. Accordingly, applicants respectfully submit that independent claim 1 and claims 2 and 6-10 that depend therefrom satisfy the written description requirement. Applicants request that the Examiner withdraw the rejection.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are in condition for allowance, which action is requested.

Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 13751-045003.

Respectfully submitted,

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